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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,050	01/25/2002	Henry Ji	25436/1124	5500

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EXAMINER	
KATCHEVES, KONSTANTINA T	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,050	JI ET AL.	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 7-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/27/03 ~~10/18/04~~*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24 are pending in the present application. Currently, claims 1 and 4-6 are under consideration.

Election/Restrictions

Applicant's election of Group I, claims 1 and 4-6, in the reply filed on 2 September 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a).

Claims 2-3 and 7-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2 September 2004.

Claim Objections

Claim 5 is objected to because of the following informalities: The word ligation is misspelled as "libation." Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuman (U.S. Patent 5,766,891) in view of Heyman *et al* (Genome Research Genome-scale cloning and expression of individual opn reading frames using topoisomerase I mediatedligation 9:383-392 1999) , Pan *et al* (Ligation of on synthetic activated DNA substrates by site-specific recombinases and topoisomerase I J. Biol Chem. 225:890-901 1993) and in view of Sambrook *et al.* (Molecular Cloning pp13-15 1982) The claims are drawn to methods of covalently linking or molecular cloning nucleic acid inserts to nucleic acid flanking molecules, which nucleic acids comprise covalently linked topoisomerase polypeptides, and which linkage method may further comprise treatment of ligated nucleic acid inserts with phosphatase for further ligation, whereby ligation occurs via a ligase, topoisomerase, by site-specific or homologous recombination, or alternatively the nucleic acid inserts are ligated into a circular cloning vector and subsequently transformed into an appropriate host cell.

Shuman teaches methods of non-directional as well as directional ligating/cloning of nucleic acids comprising mono-, bi- or trivalent linkers for topoisomerase mediated ligation of nucleic acid inserts with flanking nucleic acid molecules, which nucleic acid molecules comprise bound topoisomerase, ligation substrate sites and recombination sites (figures 7 and 8; column 1, lines 19-52; column 5, line 39-column 10, line 47).

Heyman *et al* teach topoisomerase mediated high throughput cloning/ligation comprising the joining of (non-phosphorylated) nucleic acid fragments to plasmid vectors, which nucleic acid fragments contain covalently bound topoisomerase and free 5'-hydroxyl termini, and whereby ligation between the nucleic acid inserts and the vectors occurs via topoisomerase ligase activity (see text and figure 1 on pages 383-384).

The primary references do not teach the removal of phosphate groups from the nucleic acid inserts using phosphatase, nor the use of recombinases for ligation reactions.

Pan *et al* teach the use of recombinases (i.e. Cre), bacteriophage integrases and topoisomerases in ligation reactions (abstract and introduction, page 3683; figure 1, page 3685; figure 4, page 3687).

Sambrook *et al* teach the removal of phosphate residues from nucleic acid termini using phosphatases (page 13-15).

It would have been obvious to one of ordinary skill in the art to ligate nucleic acid inserts to flanking nucleic acid molecules, including cloning vectors, using (covalently linked) topoisomerase because topoisomerase mediated ligation and cloning had been taught previously by Shuman and Heyman *et al.* One of ordinary skill in the art would have been motivated to attach topoisomerase to the nucleic acid molecules to be joined because it had been taught

previously by Shuman and Heyman *et al* that attaching topoisomerase to the end of nucleic acid molecules to be joined promoted their ligation by enhancing the accessibility of the ligation substrate sites to the topoisomerase molecule. It would have been obvious to one of ordinary skill in the art to directionally clone or ligate nucleic inserts using vectors or vector arms bearing 5'-phosphate groups, since it was known in the art that the removal of phosphate from the nucleic acid termini is required for ligation. One of ordinary skill in the art would have expected that the resulting free ends of a topoisomerase bearing vector comprising a topoisomerase mediated, nucleic acid insert is ligated together to obtain a circular vector (i.e. cloning vector) using either a ligase, topoisomerase or recombinase because the vector provided the appropriate substrates for such ligases as recombinases, topoisomerases or integrases, as had been taught by Pan *et al*, or was a routine matter in the art in the case of using traditional ligases.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (571) 272-0768. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday 7:30 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Konstantina Katcheves
Examiner
Art Unit 1636

JAMES KETTER
PRIMARY EXAMINER